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RESEARCH ARTICLE

Motor cortex representation of deep and superficial neck flexor muscles in individuals with and without neck pain

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Abstract

Sensorimotor control of neck muscles differs between individuals with and without pain. Differences in the primary motor cortex (M1) maps of these muscles may be involved. This study compared M1 representations of deep (DNF) and superficial (SNF) neck flexor muscles between 10 individuals with neck pain (NP) and 10 painfree controls. M1 organisation was studied using transcranial magnetic stimulation (TMS) applied to a grid over the skull and surface electromyography of DNF (pharyngeal electrode) and SNF. Three-dimensional maps of M1 representation of each muscle were generated. Peaks in the SNF map that represented the sternocleidomastoid (SCM) and platysma muscles were identified. Unique centre of gravity (CoG)/map peaks were identified for the three muscles. In comparison to painfree controls, NP participants had more medial location of the CoG/peak of DNF, SCM, and platysma, greater mediolateral variation in DNF CoG (p = 0.02), fewer SNF and DNF map peaks (p = 0.01). These data show that neck flexor muscle M1 maps relate to trunk, neck, and face areas of the motor homunculus. Differences in M1 representation in NP have some similarities and some differences with observations for other musculoskeletal pain conditions. Despite the small sample size, our data did reveal differences and is comparable to other similar studies. The results of this study should be interpreted with consideration of methodological issues.

KEYWORDS

electromyography, motor cortex, neck pain, transcranial magnetic stimulation

1 | INTRODUCTION

Neck pain (NP) is common and a leading cause of disability (Gbd, Injury, & Prevalence, 2016) that is reported annually by 25–50% of workers worldwide (Côté et al., 2009; Hogg-Johnson et al., 2009). Identification of effective treatments is essential. Of the many treatment approaches proposed for NP, exercise to train the neck muscles has shown promising effects on pain and disability (Falla, O'Leary, Farina, & Jull, 2012; O'leary, Falla, Elliott, & Jull, 2009). Positive outcomes have been shown for training programs that include exercise to change the coordination between neck muscles (Falla et al., 2012) using low load craniocervical flexion (Jull, Falla, Vicenzino, & Hodges, 2009). This training is based on differences in muscle activation between people with and without NP (Falla et al., 2012). Understanding the neural mechanisms underlying these differences should help refine treatments.

Control of the neck depends on coordination of multiple multilayered muscles (Conley, Meyer, Bloomberg, Feeback, & Dudley, 1995). Optimal function involves coordinated activation of flexor and extensor muscles, and muscles that are superficial and deep (Conley et al., 1995; Siegmund, Blouin, Brault, Hedenstierna, & Inglis, 2006). In relation to the neck flexors, the contributions of superficial (SNF) and deep (DNF) neck flexor muscles differ; the superficial sternocleidomastoid (SCM) muscles primarily produce torque for cervical flexion, ipsilateral side flexion, and contralateral rotation (Siegmund et al., 2006), whereas DNF muscles (e.g., longus colli and longus capitis) control segmental alignment and work with multifidus to maintain the cervical lordosis (Mayoux-Benhamou et al., 1994). Activity is biased to the DNF muscles during craniocervical flexion (Conley et al., 1995; Falla, Jull, Dall'Alba, Rainoldi, & Merletti, 2003).

Studies of several NP subgroups show spatiotemporal characteristics of neck flexor muscle activation that differ from painfree individuals (Falla, Bilenkij, & Jull, 2004; Falla, O'leary, Farina, & Jull, 2011). Whiplash-associated disorders are characterised by augmented activation of SNF muscles (e.g., SCM) during craniocervical flexion (Sterling,

Jull, Vicenzino, Kenardy, & Darnell, 2003). Compared to painfree individuals, idiopathic NP involves lower activation of DNF muscles during craniocervical flexion, greater activation of SCM during repetitive arm movements (Falla, Bilenkij, & Jull, 2004), and delayed activation of DNF muscles during rapid voluntary arm movements (Falla, Jull, & Hodges, 2004). Neural mechanisms underlying these changes have not been identified yet.

Control of the neck involves multiple networks/mechanisms at multiple levels of the sensorimotor system. The representation of the muscles in the somatotopically organised primary motor cortex (M1) provides some insight into the neural control of muscles and movements, such as mechanisms for intermuscle coordination (e.g., Massé-Alarie, Bergin, Schneider, Schabrun, & Hodges, 2017), and is modified in several chronic musculoskeletal pain conditions (Elgueta-Cancino, Schabrun, & Hodges, 2018; Schabrun, Elgueta-Cancino, & Hodges, 2015; Schabrun, Hodges, Vicenzino, Jones, & Chipchase, 2014; Shanahan, Hodges, Wrigley, Bennell, & Farrell, 2015; Tsao, Danneels, & Hodges, 2011b). Using transcranial magnetic stimulation (TMS) applied to a grid over the scalp, studies in chronic low back pain have demonstrated that the locations that induce the highest response of deep muscles of the lumbar spine differs from those observed in controls (Tsao, Galea, & Hodges, 2008). Differences in the 'volume' of the maps (Schabrun et al., 2014; Tsao et al., 2011b) and convergence between the M1 representations of superficial and deep paraspinal muscles (Schabrun et al., 2014; Tsao et al., 2011b) have also been reported. Some M1 changes have been found to relate to function (e.g., M1 map of transversus abdominis correlates with delayed activation of this muscle during rapid arm movements; Tsao et al., 2008) and features of the M1 map of back muscles relate to coordination of back movements (Elgueta-Cancino et al., 2018). The representation of neck muscles in M1 has been studied for superficial muscles [trapezius (Potter-Baker et al., 2016); and SCM/platysma (Thompson, Thickbroom, & Mastaglia, 1997)] in painfree participants. No studies have investigated the M1 representation of DNF or any muscle in individuals with NP. This study aimed to map the motor cortex representation of DNF and SNF, and to test the hypothesis that these maps would differ between individuals with and without idiopathic NP.

2 | METHODS

2.1 | Participants

Ten individuals with (three males; 29 [8] years; mean [*SD*]), and 10 without (seven males; 32 [7] years) a history of chronic NP (more than 3 months) were recruited over an 18-month period from the University community and physiotherapy clinics via newsletters, social media, posters, and word of mouth. Participants with NP were included if they reported bothersome pain in the neck region that had an intensity sufficient to interrupted their daily function as defined by at least 'moderate' disability on the neck disability index (NDI >20%) (Vernon & Mior, 1991). Participants were to report pain of idiopathic origin that had a duration of more than 3 months, although not necessarily pain every day. They were excluded if their current episode of NP related to a traumatic event (e.g., whiplash injury) or they had major spinal pathology (e.g., tumour, infection, fracture, dislocation, inflammatory disease), nerve root compromise, and previous/scheduled spinal surgery. They were not excluded if they reported concurrent headache of arm pain, but the neck had to be the major complaint.

Painfree control participants were included if they had no history of NP that had limited function or required intervention from a health practitioner. They could have no history of NP or recent history (previous 3 months) of limb pain with an intensity greater than 3/10 on a numeric rating scale (NRS). Participants were excluded from either group if they were pregnant, had an allergy to anaesthetic agents, or major neurological, cardiovascular or respiratory conditions. Participants completed the TMS safety questionnaire (Wassermann, 1998) and those who did not fulfil the criteria (e.g., history of epilepsy) were excluded (Najib & Horvath, 2014). The institutional Medical Research Ethics Committee approved the study and all participants provided written informed consent. The sample size was limited by the combination of the invasive recordings of DNF muscle activity with an oropharyngeal electrode (described below) and the high TMS intensities required to generate reliable maps of M1, but it is similar to that used in other studies that have successfully evaluated neck muscle M1 representations (Thompson et al., 1997).

2.2 | Electromyography

Electromyography (EMG) recordings were made from the right DNF and SNF muscles. Previous studies have identified that the motor evoked potentials (MEPs) recorded with surface EMG electrodes placed over the SCM muscle also include a contribution from the platysma muscle, which has a different cortical representation (Thompson et al., 1997). Thus, in the main analysis for this study, the MEP was considered to represent the combined cortical representation of these two superficial muscles and referred to as SNF. We also undertook analysis that aimed to discriminate the two areas of representation [see 'Individual muscle HS location' section]. Following the protocol described by Falla et al. (2006), DNF EMG was recorded with a custom bipolar electrode inbuilt into a nasopharyngeal catheter which was inserted via the nose to lay against the posterior oropharyngeal wall adjacent to the uvula (C2-C3 level). Surface electrodes (Ag/AgCl) were placed over the SCM muscle one-third of the distance from the mastoid process to the clavicular insertion. Pilot tests showed that this location involved the least interference from the TMS field. EMG artefacts caused by TMS interfered with detection of DNF MEP. As no TMS responses of DNF have been reported previously, our method was guided by TMS responses in the scalene muscles which are expected to have a similar conduction distance, with a mean and *SD* latency of 8.3 (1.2) to 9.7 (1.2) ms (Lissens & Vanderstraeten, 1996). Additionally, latencies of the SCM MEPs range from of 6.9 (0.7) ms (Berardelli et al., 1991) to 10.1 (1.2) ms (Hanajima et al., 1998). Thus, no response of the neck muscles was expected <6 ms after the TMS pulse. The EMG signal was suppressed between 0 and 5 ms after the stimulation, to reduce the impact of the interference of TMS pulse (Gooden, Ridding, Miles, Nordstrom, & Thompson, 1999). EMG data were preamplified 2,000 times, band-pass filtered (20–1,000 Hz) and sampled at 2,000 Hz using a Power 1401 Data Acquisition System with Signal 2 software (Cambridge Electronic Design, CED, UK).

2.3 | Cortical mapping

Single-pulse monophasic TMS was used to evaluate the representation of the neck muscles at the motor cortex (M1 map) (Magstim 2002; Magstim Company, Whitland, UK) during gentle isometric activation of the neck muscles. TMS procedures adhered to the TMS checklist of methodological quality (Chipchase et al., 2012). A figure-of-eight coil (7-cm diameter) was used with the handle orientated parallel to sagittal plane over the scalp. As previously described for other neck muscles (SCM/platysma), DNF motor threshold was close to 100% of stimulator output and as such, a standardised stimulation at 120% of motor threshold was not possible as it exceeded 100% stimulator output. For this reason, stimulator output was set at 100% for all participants. Spatial orientation for the TMS mapping was controlled using Brainsight 2 navigation system (Rogue Research Inc., Montreal, Canada) based on points of reference determined using the international 10/20 electrode placement system (Jasper, 1958). With the participants in sitting, stimulation was delivered over the left hemisphere at points referenced to the vertex location. To determine the area of muscle representation, stimuli started 8–12 cm lateral to the vertex in the interaural line as this has been identified to induce the greatest response of SNF muscles to TMS using surface EMG (Thompson et al., 1997). Five stimuli (interstimulus interval: ~5 s) were applied at each site, and the map borders were determined by delivery of pulses at 1-cm intervals moving away from the initial location in four directions (anterior, posterior, medial, and lateral) until less than three MEPs were identified from five stimuli. TMS was applied during gentle isometric activation of the neck flexor muscles matched to 10% of the EMG recorded during three repetitions of a maximal voluntary contraction (MVC) in craniocervical flexion for 3 s (60 s rest between repetitions) which involved pushing down against a pad located under the chin. The target activation during TMS was set at 10% of MVC for the SNF muscle with visual feedback provided on a screen using customised signal software.

2.4 | Data analysis

2.4.1 | Motor cortex (M1) map analysis

EMG data were exported and analysed with MATLAB 13 (MathWorks, Natick, MA). Maps of M1 were generated from the DNF and SNF EMG recordings. EMGs were full-wave rectified, trials at each scalp site averaged, and the onset and offset of the averaged MEPs were determined visually. Responses, that began less than 8 ms after the stimulus, were considered artefacts and not included in the analysis. MEP amplitude was quantified as the root mean square (RMS) EMG amplitude for the period between onset and offset of the MEP, and the background RMS EMG amplitude recorded between 55 and 5 ms before the TMS pulse was subtracted. RMS EMG amplitudes of the MEP were superimposed over a grid representing the scalp sites to produce a topographical map of the amplitude of responses. Response amplitudes were normalised to the greatest MEP amplitude 'hot spot' (HS) and values <25% of the peak were removed. The remaining responses were rescaled from 0 to 100% (Tsao et al., 2008).

Map volume was calculated as the sum of the normalised MEPs recorded across all scalp sites in which MEPs exceeded a 25% threshold. The weighted amplitude of the centre of the map [centre of gravity (CoG)] was calculated using the formula: $\mathrm{CoGx} = \sum z_i x_i / \sum z_i$; $\mathrm{CoGy} = \sum z_i y_i / \sum z_i$, where x_i refers to the scalp sites in the medial–lateral direction (x-coordinate), y_i in the anterior–posterior direction (y-coordinate), and z_i (amplitude) (Tsao et al., 2008). As previous mapping studies of spinal muscles showed large intersubject variability in muscle representation in people with and without pain (Elgueta-Cancino et al., 2018; Massé-Alarie et al., 2017), intersubject variability was quantified by subtracting the CoG for each participant from the mean CoG of the group (referred to as *CoG variation*) for each of mediolateral and anterior–posterior directions. The distance between the locations of the CoG of DNF and SNF (*CoG vector distance*) was calculated. The distance between CoG for each muscle was also calculated separately for the mediolateral and anteroposterior directions.

Individual muscle HS location

The HS for DNF was identified as the site with the largest peak in the TMS map. As a separate subanalysis, we explored all peaks in the SNF TMS map to identify peaks that could be considered to relate to SCM and platysma. On the basis of findings of Thompson et al. (1997), the largest medial peak/HS was considered to represent SCM (HS SCM; expected to lie between 0–6 cm lateral to the vertex) and the largest lateral peak/HS was considered to represent platysma (HS platysma; expected to lie between 7 and 12 cm lateral to the vertex range). To provide additional confidence that the HSs represented separate muscles, we confirmed that each was generated from MEPs with unique waveforms, as evidence of generation from a different muscle source. Waveform shapes from each peak were compared and overlayed to enable confirmation of differences in morphology (amplitude and timing). If this criterion was satisfied, the locations of the selected peaks were used to estimate the distance between the CoG of DNF and the HS of SCM and platysma.

Discrete *peaks* in the maps were defined as the grid sites at which: the amplitude of an MEP was greater than 50% of the largest MEP in the map; the peak was surrounded by seven of eight scalp sites with MEP amplitude that were at least 5% smaller than the peak; and the peak was not on a grid site adjacent to another peak (Schabrun et al., 2014).

Overlap between map representations of DNF and SCM was calculated as the number of grid sites or 'area' with MEPs (active sites) for both muscles, as a proportion of the total number of sites with an MEP of either muscle (Massé-Alarie et al., 2017).

Participants with NP rated their current pain intensity on the day of the assessment using an 11-point NRS anchored with 'no pain' at 0 and 'worst pain imaginable' at 10.

2.5 | Statistical analysis

Normality of distribution of all variables was tested with Shapiro–Wilk's test. When distribution of the variables was not normal, data were transformed. M1 map variables [map volume, CoG location, HS location, CoG DNF/SNF distance, CoG DNF/HS SCM and platysma distance, CoG variation, coordinates of CoGx/HSx and CoGy/HSy (mediolateral and anterior–posterior directions), number of discrete peaks, and overlap] were compared between groups (NP vs. painfree) and muscles (DNF and SNF or SCM and platysma, as appropriate) or coordinates (x and y) using separate two-way ANOVAs. Post hoc comparisons were performed with Duncan's multiple range tests. Relationships between pain intensity, NDI, and map representation measures

TABLE 1 Group data and statistical analysis for motor cortex features

	Painfree group		NP group		Main effects		
Variable	Mean	*n*	Mean	*n*	Group	Muscle/coordinate	Interaction effect
Discrete peaks DNF	4.0 (1.9)	10	3.1 (1.2)	10	0.02	0.03	0.62
Discrete peaks SNF	3.5 (1.9)	10	2.0 (1.1)	10			
Overlap	46 (21)	10	33 (20)	10	0.15		
Area DNF[a]	35.8 (14.9)	10	33.0 (11.2)	10	0.24	0.01	0.69
Area SNF[a]	25.7 (13.9)	10	19.0 (15.0)	10			
Vol DNF[a]	12.8 (6.3)	10	10.7 (5.4)	10	0.18	0.04	0.79
Vol SNF[a]	9.2 (5.2)	10	7.1 (6.4)	10			
Hotspot DNF	8.0 (2.3)	10	6.4 (2.2)	10	0.03	0.13	0.99
Hotspot SNF	6.9 (2.8)	10	5.3 (1.4)	10			
DNF *x*—coordinates	7.3 (2.4)	10	6.2 (2.2)	10	0.08	0.23	0.83
SNF *x*—coordinates	6.6 (2.6)	10	5.2 (1.5)	10			
DNF *y*—coordinates	2.2 (2.3)	10	0.3 (1.6)	10	0.03	0.16	0.29
SNF *y*—coordinates	0.8 (2.0)	10	0.1 (0.9)	10			
CoG DNF vector	7.3 (1.0)	10	6.5 (2.0)	10	0.04	0.15	0.62
CoG SNF vector	6.8 (2.1)	10	5.4 (1.4)	10			
DNF *x*—coordinates	7.0 (1.0)	10	6.4 (2.0)	10	0.05	0.18	0.58
SNF *x*—coordinates	6.7 (2.0)	10	5.4 (1.4)	10			
DNF *y*—coordinates[a]	1.4 (1.2)	10	0.8 (0.8)	10	0.04	0.10	0.91
SNF *y*—coordinates[a]	0.9 (1.0)	10	0.2 (0.5)	10			
CoG variation DNF vector	1.2 (0.9)	10	1.8 (1.0)	10	0.32	0.85	0.15
CoG variation SNF vector	1.8 (1.2)	10	1.3 (0.7)	10			
DNF *x*–coordinates	0.7 (0.6)	10	1.6 (1.0)	10	0.18	0.98	0.03
SNF *x*—coordinates	0.8 (0.8)	10	0.7 (0.4)	10			
DNF *y*—coordinates	1.5 (1.1)	10	1.1 (0.8)	10	0.64	0.63	0.60
SNF *y*—coordinates	0.7 (0.7)	10	0.4 (0.3)	10			
CoG vector distance DNF/SNF	1.7 (0.9)	10	2.4 (1.2)	10	0.12		
DNF/SNF *x*—coordinates	1.4 (0.8)	10	2.3 (1.2)	10	0.12	0.001	0.058
DNF/SNF *y*—coordinates	0.8 (0.6)	10	0.7 (0.6)	10			
HS SCM *x*—coordinates	5.6 (1.5)	10	3.8 (1.4)	10	0.002	0.001	0.35
HS platysma *x*—coordinates	9.3 (0.9)	10	8.3 (1.3)	10			
HS SCM *y*—coordinates	0.3 (1.3)	10	−0.2 (1.1)	10	0.25	0.01	0.79
HS platysma *y*—coordinates	2.1 (2.0)	10	1.3 (2.2)	10			
Distance CoG DNF/ HS SCM							
x—coordinates	1.7 (1.4)	10	2.6 (1.7)	10	0.21		
y—coordinates	1.2 (1.0)	10	1.1 (0.6)	10	0.84		
Distance CoG DNF/HS platysma							
x—coordinates	2.2 (0.7)	10	2.1 (1.3)	10	0.95		
y—coordinates	1.3 (1.1)	10	1.5 (1.3)	10	0.71		

[a]Root square transformation.
CoG = centre of gravity; DNF = deep neck flexor; HS platysma = SNF lateral peak; HS SCM = SNF medial peak; NP = neck pain; SCM = sternocleidomastoid; SNF = superficial neck flexor; Vol = volume of the map.

were investigated using Spearman's rank. Significance was set at $p < 0.05$. Data are presented as mean and *SD* (mean [*SD*]) throughout the manuscript, unless otherwise indicated.

3 | RESULTS

3.1 | M1 organisation of neck muscles in painfree participants

MEPs were successfully recorded for DNF and SNF for all participants (Table 1).

Group averaged representations of DNF and SNF are shown in Figure 1. The area of maximal activity (HS) for DNF was identified 7.3 [1.9] cm lateral and 1.7 [2.1] cm anterior to the vertex. The average CoG of DNF was located 7.1 [1.0] cm lateral and 1.4 [1.2] cm anterior to the vertex, and CoG of SNF was 6.7 [2.0] cm lateral and 0.9 [1.0] anterior to the vertex. The location of CoG was not different between DNF and SNF in the medial–lateral (CoG *x*-coordinate: main effect—muscle $F_{(1,\ 18)} = 0.38$, $p = 0.55$) or anterior–posterior directions (CoG *y*-coordinate: main effect—muscle $F_{(1,\ 18)} = 0.9$, $p = 0.37$; Figure 2). Separate medial and lateral peaks in the SNF map could be identified (generated from MEPs with different waveforms) in all painfree participants. In

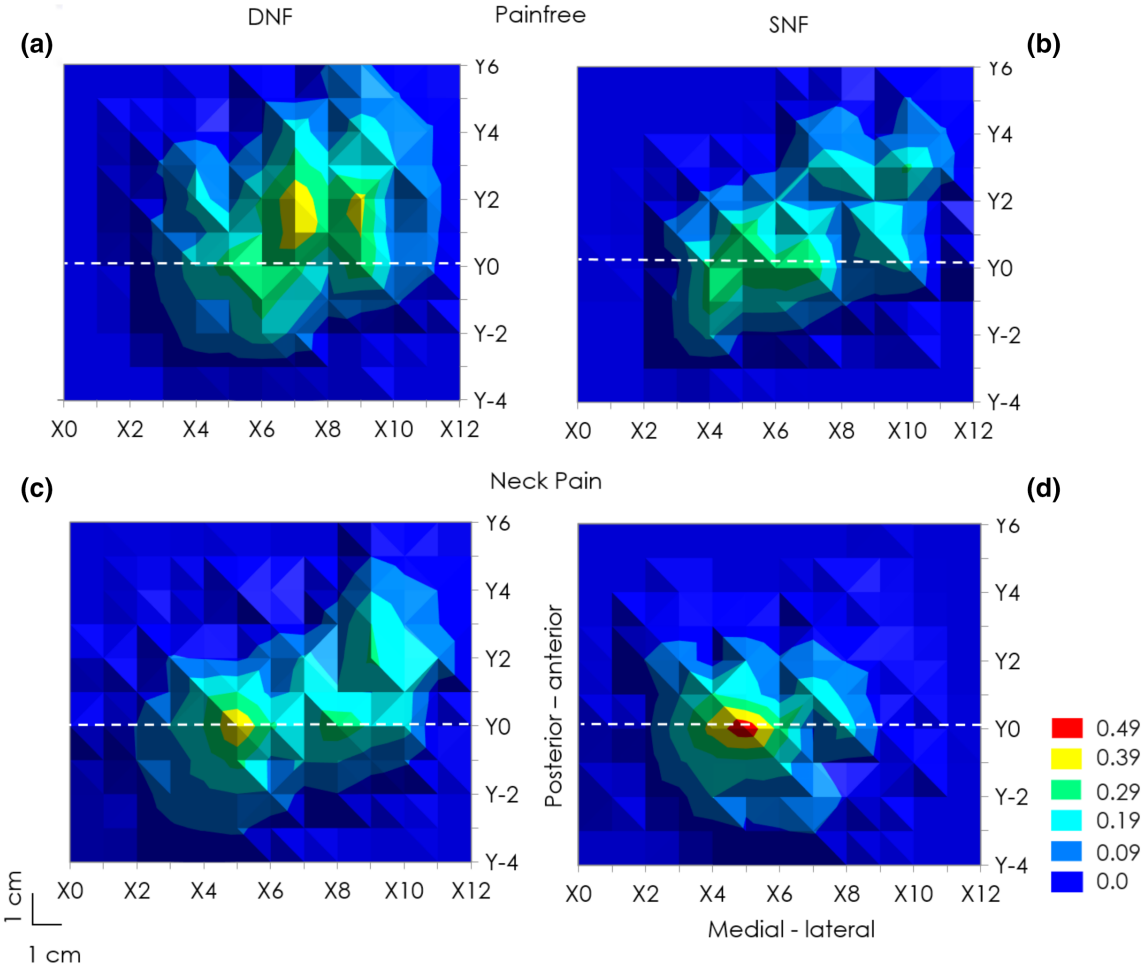

FIGURE 1 Group average of the normalised M1 maps aligned to the anatomical reference point (vertex). The dashed lines indicate the location of vertex (vertex 0.0). Data are shown for painfree (a, b) and neck pain (c, d) groups. Left panels present deep neck flexors muscles (DNFs; a, c) and right panels superficial neck flexors muscles (SNFs; b, d). The coloured scale indicates the amplitude as a proportion of the magnitude of the largest motor evoked potential [Color figure can be viewed at wileyonlinelibrary.com]

4/10 painfree participants (and 3/10 NP participants, see below) additional peaks could be identified between the main medial and lateral peaks that were attributed to SCM or platysma. In general, these were generated from MEPs that were consistent with summation of the distinct MEP waveforms that were identified for the SCM and platysma HS (Figure 3). The main peak attributed to SCM was located 5.6 [1.5] cm lateral and 0.3 [1.3] cm anterior to the vertex, and that for platysma 9.3 [0.9] cm lateral and 2.1 [2.0] cm anterior to the vertex. The locations were different between muscles in the medial–lateral [main effect—muscle $F_{(1,\ 18)} = 43.2$, $p = 0.0001$] and anterior–posterior directions [main effect—muscle $F_{(1,\ 18)} = 5.5$, $p = 0.03$].

The CoG of DNF was further from vertex than HS SCM (*x*-coordinate: main effect—muscle $F_{(1,\ 18)} = 7.3$, $p = 0.02$) and closer to the vertex than HS platysma (*x*-coordinate: main effect—muscle $F_{(1,\ 18)} = 6.7$, $p < 0.001$) in the mediolateral direction (Figure 2). The location of the DNF CoG did not differ significantly from HS SCM and HS platysma in anterior–posterior direction (CoG DNF *y*-coordinates: SCM main effect—muscle $F_{(1,\ 18)} = 3.5$, $p = 0.08$; platysma main effect—muscle $F_{(1,\ 18)} = 1.0$, $p = 0.33$).

The map volumes of DNF and SNF did not differ for painfree participants [main effect—muscle $F_{(1,\ 18)} = 2.1$, $p = 0.17$] and presented similar number of discrete peaks for SNF and DNF maps [main effect—muscle $F_{(1,\ 18)} = 0.8$, $p = 0.63$, Figure 4]. There was 46% overlap between DNF and SNF representations.

3.2 | M1 organisation of neck muscles in participants with NP

The HS DNF was located 6.1 [2.0] cm lateral from the vertex and 0.3 [1.6] cm anterior from the interaural line. The CoG for DNF was located 6.4 [2.0] cm lateral and 0.8 [0.8] cm anterior to the vertex and that of SNF was 5.4 [1.4] cm lateral and 0.3 [0.5] cm anterior to the vertex and did not differ significantly from each other in either direction (Figure 2). Similar to the painfree group, it was possible to identify a medial and lateral peak with different MEPs waveforms obtained from SNF maps in all NP participants. HS SCM was located 3.8 [1.4] cm lateral and −0.2 [1.1] cm anterior to the vertex, and HS platysma was located 8.3 [1.3] cm lateral and 1.3 [2.2] anterior to the vertex. The HS SCM was located significantly more medial than HS platysma [main effect—muscle $F_{(1,\ 18)} = 57.5$, $p < 0.001$]. There was no difference in the anterior–posterior direction [main effect—muscle $F_{(1,\ 18)} = 3.6$, $p = 0.07$].

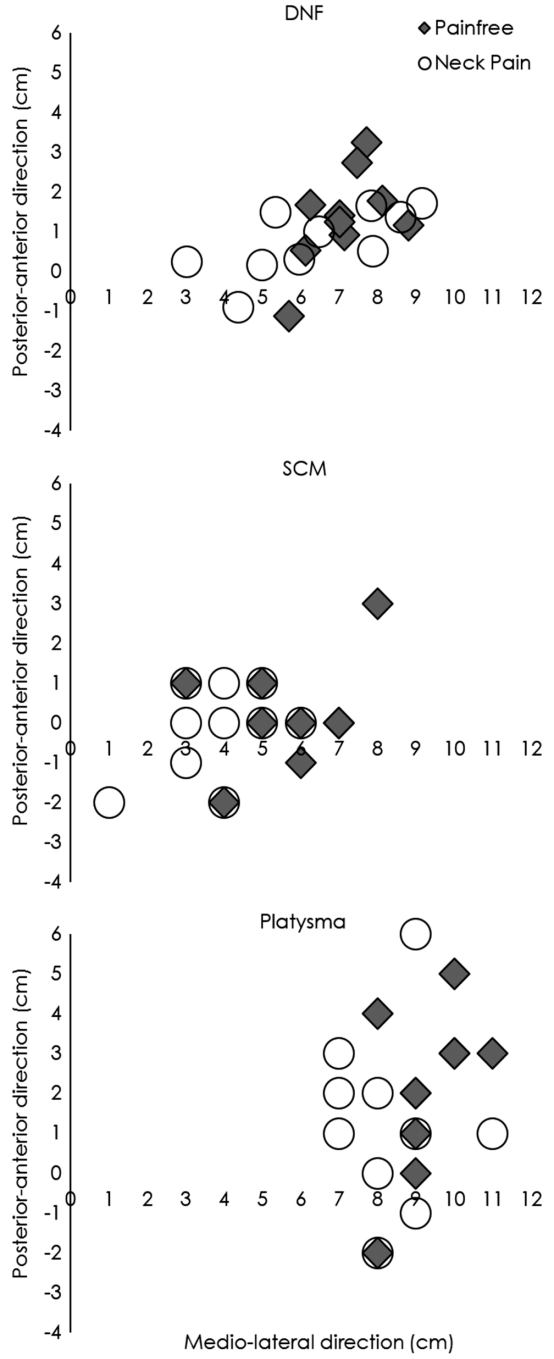

FIGURE 2 Individual data of location of centre of gravity (CoG) of deep neck flexor (DNF) muscles (top panel), the hot spot (HS) for sternocleidomastoid (SCM) (middle panel) muscle and the HS of platysma (bottom panel) muscle are plotted in the mediolateral and anteroposterior direction for neck pain (NP) and painfree group. Note the medial shift of the location of NP group relative to painfree controls, large variability of DNF CoG in the mediolateral direction location in NP group and distinct location of SCM (medial) and platysma (lateral) HSs

In the medial–lateral direction, the location of CoG of DNF was lateral to HS SCM and medial to HS platysma, and differed significantly from both (*x*-coordinate: CoG DNF vs. HS SCM: main effect—muscle $F_{(1,\ 18)} = 11.3$, $p = 0.004$; CoG DNF vs. HS platysma: main effect—muscle $F_{(1,\ 18)} = 6.7$, $p = 0.02$). In anterior–posterior direction, the CoG DNF was more anterior than HS SCM [main effect—muscle $F_{(1,\ 18)} = 4.6$, $p = 0.05$] but it was not different to HS platysma [main effect—muscle $F_{(1,\ 18)} = 0.5$, $p = 0.48$].

Map volume of DNF did not differ from that of SNF [main effect—muscle $F_{(1,\ 18)} = 2.7$, $p = 0.12$]. There was a greater number of discrete peaks for DNF than SNF [main effect muscle $F_{(1,\ 18)} = 4.8$, $p = 0.04$, Figure 4] and 33% overlap of representation of DNF and SNF maps.

3.3 | Comparison of M1 organisation of neck muscles between groups

Results of statistical comparison of M1 features between groups are presented in Table 1.

3.3.1 | Location of the M1 representations

The CoG of DNF and SNF maps was located more medial and more posterior for NP than painfree participants (Table 1; Figure 1). The NP group also had a more medial placement of the HS SCM and HS platysma than the painfree group. There was no difference between groups in the location of HS SCM and HS platysma in the anterior–posterior direction.

The NP group showed a larger intersubject variation in the location of CoG for DNF between individuals along mediolateral direction (CoG *variation*: *x*-coordinates) (post hoc $p = 0.03$), but not for SNF ($p = 0.56$). Variation of CoG location in anteroposterior direction did not differ between NP and painfree groups (Figure 2).

3.3.2 | Overlap between M1 representations

There was no difference in area of overlap between DNF and SNF maps (Table 1). However, data inspection revealed the presence of an outlier in the NP group (more than 2 *SD* from the mean) and when the analysis was repeated without the outlier, the comparison between groups showed a significantly smaller overlap for NP group [main effect group $F_{(1,\ 17)} = 5.8$, $p = 0.03$].

Although the vector distance between CoGs of DNF and SFN did not differ between groups, the distance was larger for both groups in the mediolateral than anteroposterior directions (Table 1). The distance between the DNF CoG and HS SCM was not different between groups in either the mediolateral or anteroposterior directions. Likewise, there was no difference in distance between CoG DNF and HS platysma in either the mediolateral or anteroposterior directions.

There was no difference between groups for the map volumes of DNF and SNF (Figure 1). There were fewer discrete peaks for the representation of DNF and SNF in the NP than painfree group (Figure 4).

4 | DISCUSSION

This study examined motor cortex organisation of neck muscles in individuals with and without idiopathic NP. The findings show three independent areas of M1 that represent the three neck flexor muscles identified in this study. There was also evidence of differences in M1 organisation between groups. Key observations were that NP involved different locations of map peaks, greater variation of DNF CoG location, and fewer peaks of M1 maps for all muscles. In contrast to closer proximity of M1 maps observed in back pain, when data from one extreme

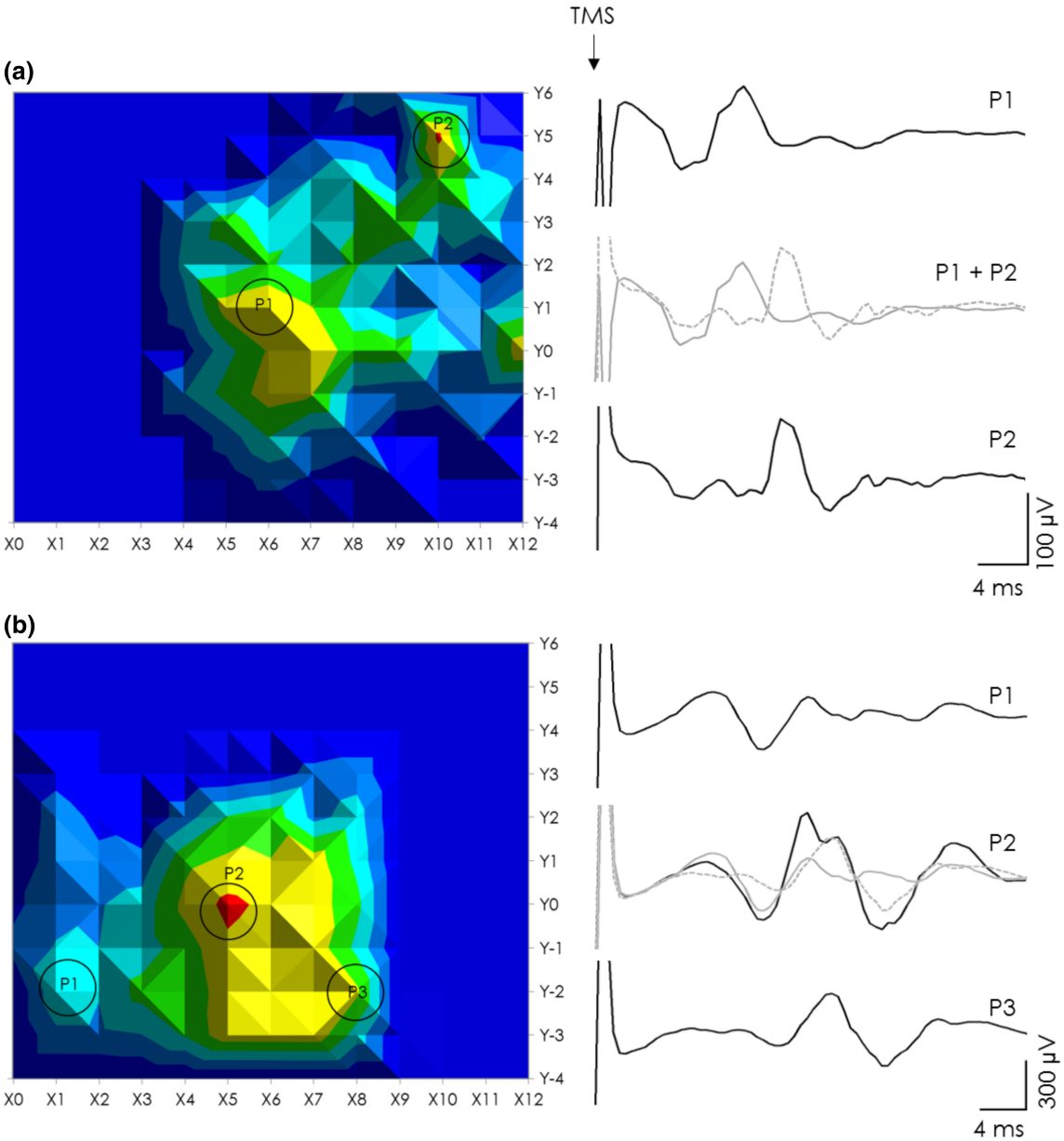

FIGURE 3 Waveform of the motor evoked potentials (MEP) attributed to sternocleidomastoid (SCM; P1) and platysma (P2) from the superficial neck flexor (SNF) electromyography recording. (a) Normalised map for SNF muscles of a representative painfree participant (left panel). Right panel shows waveforms of the MEPS that were located at the grid sites related to the peaks attributed to the hot spots for SCM and platysma. (b) Normalised map for SNF muscles of a separate representative participant who demonstrated an additional intermediate peak (left panel). Right panel shows the MEP waveforms of three peaks; (P1) MEP waveform attributed to SCM, and (P2) MEP waveform attributed to platysma, and additional peak (P3) that was generated from MEPs that shared morphology of that for P1 and P2 and was interpreted to represent summation of the MEP waveforms of SCM and platysma in this participant. The grey traces represent P1 (continuous) and P2 (discontinuous) waveforms overlapped [Color figure can be viewed at wileyonlinelibrary.com]

participant was excluded, NP was characterised by less overlap between DNF and SNF M1 representations. The large variation could imply different subgroups in the nature of motor cortex changes.

Although the extensors muscles contribute to the stability and mobility of the neck in conjunction with the flexor muscles, these muscles were not included in the present study. Evaluation of M1 maps of the extensor muscles would require separate trials with a different task to control pre-activation [because erector spinae muscles have shown to have high stimulation threshold (Ferbert, Caramia, Priori, Bertolasi, & Rothwell, 1992; O'Connell, Maskill, Cossar, & Nowicky, 2007; Strutton, Theodorou, Catley, McGregor, & Davey, 2005; Tsao, Danneels, & Hodges, 2011a)] and a different coil orientation. Further, the anatomical configuration of the neck extensors muscles means that intramuscular electrodes are required to record from separate muscle layers (Bexander, Mellor, & Hodges, 2005), and this would not be feasible in an already invasive study. Future work should investigate the extensor muscles in people with and without NP.

4.1 | M1 representation of neck muscles in painfree individuals

In general, TMS M1 maps are broadly consistent with the classical organisation of the motor homunculus proposed by Penfield (1954).

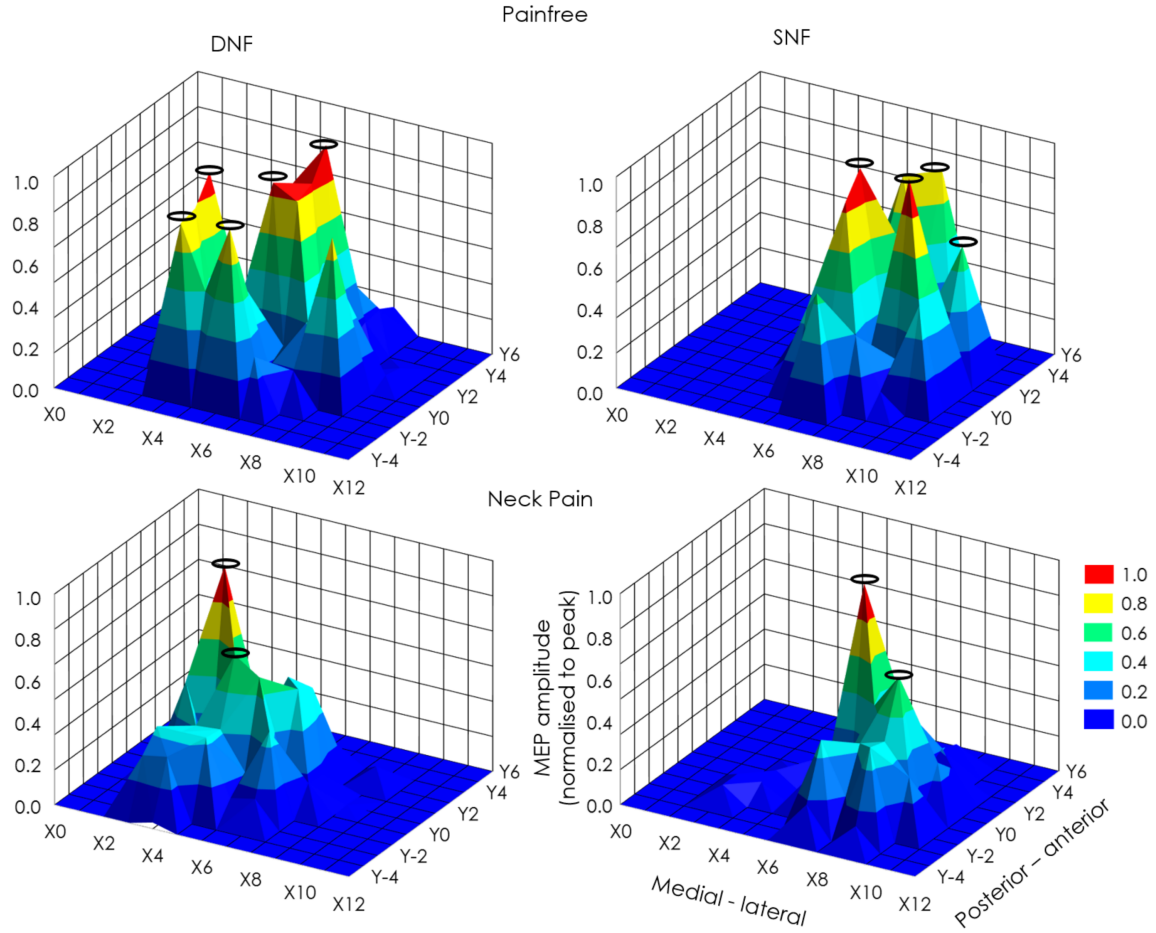

FIGURE 4 Three-dimensional representations of motor maps of deep neck flexor (DNF) and superficial neck flexor (SFN) muscles of a representative painfree and neck pain (NP) participant. Black circles highlight the discrete 'peaks' identified in the M1 maps according to the a priori defined criteria. Note the smaller number of peaks in the M1 maps for the NP participant [Color figure can be viewed at wileyonlinelibrary.com]

Few studies have investigated M1 maps of lumbar (Schabrun et al., 2015; Tsao & Hodges, 2008; Tsao, Tucker, & Hodges, 2011) and neck (Thompson et al., 1997) muscles. This is the first study to investigate the M1 representation of deep neck muscles. The results confirm previous evidence (Thompson et al., 1997) of separate representations for two SCM muscles (~4 cm lateral to the vertex) and platysma (~8 cm lateral to the vertex). We add new data of the M1 representation of the DNF muscles at ~7 cm lateral to the vertex, between the superficial muscle representations. When referenced to the motor homunculus-based Penfield (1954) data, it is tempting to speculate that this organisation has functional significance. The classical homunculus presents an unusual situation for the neck, which is represented by three areas: a medial area proximal to the trunk representation; a lateral area representing anterior structures of the throat/face; and an intermediate 'neck' region adjacent to the shoulder representation (Figure 5). Our data imply the HS SCM approximates the proximal trunk area, close to the M1 representations of upper trapezius and splenius capitis (Alexander, Miley, Stynes, & Harrison, 2007; Berardelli et al., 1991), as well as scalene and intercostal muscles (Lissens & Vanderstraeten, 1996), which lie 4–6 cm from the vertex. DNF approximates the 'neck' area, and HS platysma approximates the face/throat area [M1 representation of face (Dubach, Guggisberg, Rösler, Hess, & Mathis, 2004; Rödel, Laskawi, & Markus, 1999; Säisänen et al., 2015), larynx and tongue (Rödel Ralph et al., 2009) muscles at 8–12 cm lateral to the vertex (Weiss et al., 2013)].

The discrete representations of these three muscles that flex the neck may has an influence in the mechanisms of control and it is plausible a functional consequence. The results concur with the hypothesis that the close proximity of representations of muscles facilitates synergist muscle control during motor actions (Cunningham, Machado, Yue, Carey, & Plow, 2013; Dechent & Frahm, 2003; Massé-Alarie et al., 2017; Plow, Arora, Pline, Binenstock, & Carey, 2010). This might explain the proximity of SCM, trapezius and scalene muscles, which share roles in neck rotation and craniocervical extension plus an auxiliary inspiratory respiratory function (Alexander et al., 2007; Berardelli et al., 1991). In contrast to SCM, the DNF muscle induces craniocervical flexion (Falla et al., 2003; Jull, O'Leary, & Falla, 2008), which may explain its separate location. Convergence of the M1 representations of platysma and facial muscles concurs with synergists role in lip and jaw depression (Hwang, Kim, & Lim, 2017).

4.2 | Motor cortex organisation differs between individuals with and without idiopathic NP

Differences in map representations in musculoskeletal pain syndromes are frequently reported (Coppieters et al., 2016). M1 map differences

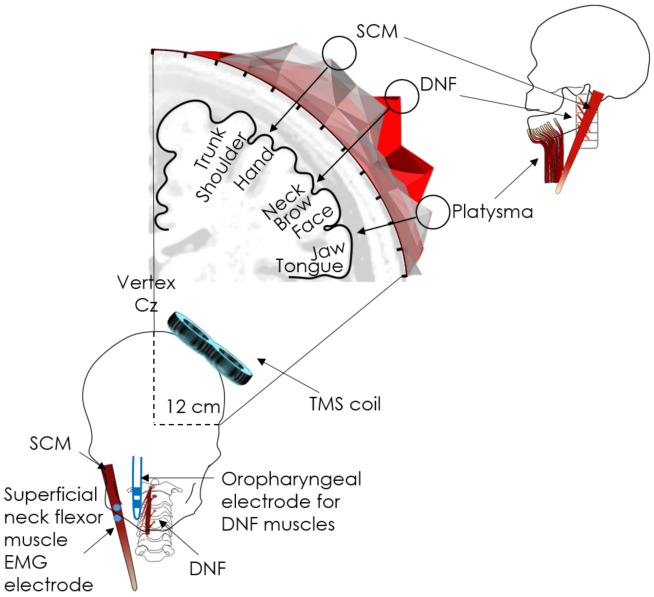

FIGURE 5 Relationship between motor cortex maps and classical motor homunculus. Muscle anatomy and sites for electromyographic recordings (bottom panel) are shown along with maps of motor evoked potentials generated with transcranial magnetic stimulation (TMS) of each site of the stimulation grid superimposed over scalp sites. Motor cortex maps are compressed in the anteroposterior direction to show only the mediolateral orientation of the maps of DNF (red) and recordings from SCM (grey) with the separate peaks attributed to sternocleidomastoid (SCM) and platysma. Maps are scaled to the grid over the scalp and to the representation of the classical organisation of the motor cortex based on the data of Penfield (1954). The open circles highlight the peaks of activation of map representations attributed to each muscle [Color figure can be viewed at wileyonlinelibrary.com]

include map size, location, and/or number of peaks, volume, and the overlap between maps for different muscles (Massé-Alarie et al., 2017; Schabrun et al., 2014; Te, Baptista, Chipchase, & Schabrun, 2017; Tsao et al., 2011b; Ziemann & Siebner, 2008). Although the importance of changes in M1 organisation is not yet fully understood, previous research has found associations between differences of some parameters are concurrent with alterations in motor control, such as delayed muscle activations (Tsao et al., 2008). This study identified group differences in some, but not all, of these M1 map parameters. The presence of these changes provides a possible mechanism underlying differences in the spatiotemporal characteristics of neck flexor muscle activation associated to NP.

First, DNF and SNF M1 maps were located more posteriorly and medially in NP, and the HS SCM and HS Platysma were more medial. Differences in location of M1 representations in other body regions have been reported in parallel with motor impairment. For instance, the amplitude of 'shift' in the deep abdominal muscle M1 map correlated with delayed activation in a postural task (arm movement; Tsao et al., 2008). Although the exact mechanism remains unclear, these changes seem to indicate a relationship between functional organisation of M1 and alterations of temporal parameters of muscle activation. We did not assess motor function, but previous work has shown delayed DNF activation in the same postural task, and altered coordination between DNF and SCM during craniocervical flexion in NP (Falla et al., 2011; Falla, Bilenkij, & Jull, 2004), which we speculate may concur with the 'shift' of the map representation of flexor muscles.

Second, unlike observations in back/knee pain, the distance between M1 representations was not reduced in NP. Although the DNF representation in NP was shifted relative to painfree controls to approximate the location of the HS SCM in painfree controls, the HS SCM was also different. Thus, the distance between DNF and SNF M1 representations did not differ, and instead (after removal of an outlier) M1 maps had less overlap. In back pain, the representation of superficial lumbar longissimus is more posterior such that it approximates the same location as the deep multifidus muscle (Schabrun et al., 2015; Tsao et al., 2011b). In patellofemoral pain, representations of rectus femoris, vastus lateralis, and vastus medialis are shifted anteriorly with greater overlap (Te et al., 2017). In back pain, greater overlap of M1 representations has been linked with less ability to separately move spine regions (Elgueta-Cancino et al., 2018; Tsao et al., 2011b). In musicians and writers with task-specific dystonia, parallel observations showed greater overlap of hand muscles M1 maps induced by highly skilled training (Byl, McKenzie, & Nagarajan, 2000; Furuya & Hanakawa, 2016; Quartarone, Siebner, & Rothwell, 2006) and compromised capacity for separate finger movement (Elbert et al., 1998). These observations could suggest a link between loss of discrete organisation of M1 and alteration of task performance. We speculated that a similar changes in M1 organisation may be present in NP, with alterations in temporal patterns of muscle activation such as compromised capacity to separately control DNF and SCM has been described (Falla, Jull, & Hodges, 2004). The failure to observe such difference implies that this feature may not have a simple interpretation related to relationship between muscle activity for all tasks but provides an insight of possible differential adaptations to the pain condition in neck muscles.

Third, NP participants had greater interindividual variation in the mediolateral DNF CoG location. Although anatomical (gyri characteristics and cell orientation) and methodological (coils orientation and anatomical landmarks) issues contribute to map variation, we argue those features are unlikely to underlie a systematic difference between groups. On the basis of other data, an alternative explanation is that CoG variation might reflect interindividual differences in motor strategy. For instance, previous work in humans has shown that location of M1 maps depends on use—variation in M1 map location varies with interindividual differences in patterns of synergist muscle coordination (Plow et al., 2014). Thus our variability of DNF M1 maps might reflect interindividual variation in strategies of motor 'compensation'. This variation may preclude identification of systematic differences in proximity of SNF/DNF M1 maps.

Fourth, DNF/SNF M1 maps had fewer peaks in NP. This has been observed in other conditions such as back (Schabrun et al., 2015; Tsao et al., 2011b) and elbow (Schabrun et al., 2014) pain. An interpretation of this difference is that lower M1 map complexity implies lower versatility of muscle control for different contexts. This is based on the assumption that discrete peaks are involved in coordination of different patterns of synergist muscle activity to subserve different functions (Massé-Alarie et al., 2017). This has been shown by differences

in location of HSs in M1 maps during activation of a muscle in different tasks [e.g., wrist extensor muscle activity to extend the wrist vs. counteraction of the wrist flexion moment of the finger flexor muscles in during gripping (Massé-Alarie et al., 2017)] and colocation of HSs of separate muscles that act synergistically for that task (Massé-Alarie et al., 2017). If true, this evidence provides basis to infer that changes at level of M1 functional organisation may influence motor performance. Consequently, fewer peaks in the neck muscle M1 representations may reduce the capacity to activate a muscle in a task-specific manner, with potential implications for motor control quality.

Finally, differences were not apparent in some map parameters that are commonly reported in musculoskeletal pain syndromes. There was no difference in map volume between groups. This might be explained by the stimulation paradigm, which involved 100% TMS intensity for all participants. This might exaggerate map volumes for some participants [i.e., map volume depends on stimulus intensity relative to the motor threshold (Thickbroom, Sammut, & Mastaglia, 1998; Uy, Ridding, & Miles, 2002)—individuals with low motor thresholds could have a larger map volume as a result of volume conduction]. Although possible, pilot tests revealed that high TMS intensity was necessary to elicit motor responses in DNF/SNF in agreement with previous reports (Thompson et al., 1997). Alternatively, these features may be condition/task specific.

It is important to note that although we observed differences in M1 representation between groups, we cannot conclude they are a precursor to NP, a consequence of NP, or occur in parallel with NP without causal link. As pain can change M1 features (Schabrun et al., 2014; Schabrun et al., 2015; Te et al., 2017; Tsao et al., 2008; Tsao et al., 2011b), and motor demands change the size of M1 muscle representations (Hund-Georgiadis & von Cramon, 1999; Pascual-Leone et al., 1995; Pascual-Leone, Amedi, Fregni, & Merabet, 2005), it is tempting to speculate that the differences represent an adaptation to pain. Longitudinal studies are required.

4.3 | Methodological limitations

The results of this study should be interpreted with consideration of several methodological issues. First, the sample size was small because of the invasiveness of the methods. Despite the small sample size, our data did reveal differences and is comparable to other similar studies, but we did identify high variation. The identification of the impact of outlier data on the interpretation of the results provides further foundation for detailed analysis of variation in future studies. Second, our NP group included a greater proportion of women than the control group. This concurs with the higher prevalence of NP in women (Fejer, Kyvik, & Hartvigsen, 2006). As some sex differences in response to pain have been identified in other work (Fillingim, King, Ribeiro-Dasilva, Rahim-Williams, & Riley, 2009; Gombatto, Collins, Sahrmann, Engsberg, & Van Dillen, 2006), this may have influenced our results and requires further consideration in future work to specifically address this issue.

4.4 | Clinical implications

There is some evidence in chronic musculoskeletal syndromes that treatments targeting motor control can change M1 organisation and reduce pain (Tsao, Galea, & Hodges, 2010). For example, training of deep abdominal muscle control in back pain shifts M1 representation and reduces pain (Tsao et al., 2010). Further, in painful dystonias, interventions that suppress abnormal muscle activation [e.g., Botox injections (Thickbroom Gary, Byrnes Michelle, Stell, & Mastaglia Frank, 2003)] and decrease pain (Schabrun, Stinear, Byblow, & Ridding, 2009) can 'normalise' M1 organisation. Similarly, interventions that target modification of primary somatosensory cortex maps reduce pain (Flor, Denke, Schaefer, & Grüsser, 2001; Moseley, Zalucki, & Wiech, 2008). Although the mechanisms underlying therapy-induced M1 changes are incompletely understood, in stroke patients, the direction of M1 organisation change depends on the gradient of intracortical disinhibition of surrounding networks (Liepert, Haevernick, Weiller, & Barzel, 2006). As motor skill training generates more focal M1 representations (Hund-Georgiadis & von Cramon, 1999; Pascual-Leone et al., 1995; Pascual-Leone et al., 2005), it is plausible that therapeutic approaches that target specific movements could restore cortical organisation. Following this logic, exercise interventions that target neck muscle coordination (Falla et al., 2012) have shown promising effects on pain/disability (Falla et al., 2012; Jull et al., 2009; O'leary et al., 2009), and may change M1 organisation.

Whether therapeutic approaches for NP that target changes in motor control of neck muscles modify M1 organisation remains unclear. Perhaps more importantly, it remains to be tested whether changes in M1 organisation are related to improved pain, disability, and NP recurrence.

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CONFLICT OF INTEREST

The authors have no conflict of interest to declare.

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